

Attorney Docket No. VPI/96-01 CIP2 DIV3

Applicants

Mark J. Batchelor et al.

For

INHIBITORS OF INTERLEUKEN-1 β CONVERTING

ENZYME

Hon. Commissioner for Patents

New York, New York 10020

July 29, 2002

P.O. Box 2327

Arlington, VA 22202

EXPRESS MAIL CERTIFICATION

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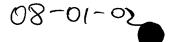
Date of Deposit: July 29, 2002

I hereby certify that this certification and the following papers:

- Transmittal Letter for Information Disclosure Statement (in duplicate);
- Information Disclosure Statement (in duplicate);
- 3. PTO Form-1449 (in duplicate)

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Name: Lillian Garcia



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VPI/96-01 CIP2 DIV3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Examiner

Not Yet Assigned

AUG (0 5 2002

Group

1624

TECH CENTER 1600/2900

Applicants

Mark J. Batchelor et al.

Application No.

10/058,522

Confirmation No.

4312

Filed

January 28, 2002

For

INHIBITORS OF INTERLEUKIN-1B CONVERTING

ENZYME

New York, New York July 29, 2002

Hon. Commissioner for Patents Washington, D.C. 20231

TRANSMITTAL LETTER FOR INFORMATION DISCLOSURE STATEMENT

Sir:

Transmitted herewith is an Information Disclosure Statement in the aboveidentified application. This Statement is submitted:

- within three months of the application filing date;
- more than three months from the application filing date but before [X] the mailing of the first Office Action on the merits.

In accordance with 37 C.F.R. § 1.97(b), submission of this Statement requires no fee. The Director is hereby authorized to charge payment of any fee required in connection with the accompanying Information Disclosure Statement to Deposit

Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

Respectfully submitted,

James F. Haley, Jr. (Reg. No. 27,794)

Attorney for Applicants

Min Wang (Reg. No. 51,303)

Kristin M. Joslyn (Reg. No. 47,692)

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January 28, 2002

For

Junuary 20, 2002

INHIBITORS OF INTERLEUKIN-1β CONVERTING ENZYME

New York, New York

July 29, 2002

Hon. Commissioner for Patents

Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97(b) and 1.98, applicants hereby make the

following documents of record in the above-identified application:

United States Patents

Inventor(s)	Patent No.	Issue Date
Jones et al.	4,276,298	June 30, 1981
Jones et al.	4,369,183	January 18, 1983

Mueller et al.	4,499,295	February 12, 1985
Mueller et al.	4,551,279	November 5, 1985
Mueller et al.	4,584,397	April 22, 1986
Dower et al.	4,968,607	November 6, 1990
Digenis et al.	5,008,245	April 16, 1991
Krantz et al.	5,055,451	October 8, 1991
Dower et al.	5,081,228	January 14, 1992
Krantz et al.	5,158,936	October 27, 1992
Dower et al.	5,180,812	January 19, 1993
Zimmerman et al.	5,374,623	December 20, 1994
Bills et al.	5,411,985	May 2, 1995
Black et al.	5,416,013	May 16, 1995
Chapman et al.	5,430,128	July 4, 1995
Chapman et al.	5,434,248	July 18, 1995
Dolle et al.	5,462,939	October 31, 1995
Zimmerman et al.	5,486,623	January 23, 1996
Mallamo et al.	5,498,616	March 12, 1996
Daumy et al.	5,498,695	March 12, 1996
Dolle et al.	5,552,400	September 3, 1996
Dolle et al.	5,565,430	October 15, 1996
Bemis	5,656,627	August 12, 1997

Bemis	5,716,929	February 10, 1998
Bemis	5,756,466	May 26, 1998
Dolle	5,585,357	December 17, 1996
Dolle	5,585,486	December 17, 1996
Dolle	5,670,494	September 23, 1997
Dolle	5,639,745	June 17, 1997

Foreign Patents or Published Applications

Inventor(s)	Publication No.	<u>Publication Date</u>
Dunlap et al.	WO 90/13549	November 15, 1990
Black et al.	W0 91/15577	October 17, 1991
Black et al.	WO 93/05071	March 18, 1993
Heng et al.	WO 93/09135	May 13, 1993
Chapman et al.	WO 93/14777	August 5, 1993
Chapman et al.	WO 93/16710	September 2, 1993
Horvitz et al.	WO 93/25683	December 23, 1993
Horvitz et al.	WO 93/25685	December 23, 1993
Horvitz et al.	WO 93/25694	December 23, 1993
Howard et al.	WO 94/00154	January 6, 1994
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Robinson	WO 94/03480	February 17, 1994

Yuan et al.	WO 95/00160	January 5, 1995
Hagmann et al.	WO 95/05192	February 23, 1995
Norman	WO 95/16706	June 22, 1995
Dolle et al.	WO 95/26958	October 12, 1995
Dolle et al.	WO 95/29672	November 9, 1995
Dolle et al.	WO 95/33751	December 14, 1995
Bemis et al.	WO 95/35308	December 28, 1995
Dolle et al.	WO 96/03982	February 15, 1996
Ryoichi et al.	WO 96/25408	August 22, 1996
Schirlin et al.	EP-A-0 275 101	July 20, 1988
Bey et al.	EP-A-0 410 411	January 30, 1991
Flynn et al.	EP-A-0 417 721	March 20, 1991
Geseilchen et al.	EP-A-0 479 489	April 8, 1992
Kiso et al.	EP-A-0 504 938	September 23, 1992
Chapman et al.	EP-A-0 519 748	December 23, 1992
Ando et al.	EP-A-0 525 420	February 3, 1993
Chapman et al.	EP-A-0 528 487	February 24, 1993
Bull et al.	EP-A-0 529 713	March 3, 1993
Chapman et al.	EP-A-0 533 226	March 24, 1993
Howard et al.	EP-A-0 533 350	March 24, 1993
Heng et al.	EP-A-0 618 223	October 5, 1994

Dolle et al.	EP-A-0 623 606	November 9, 1994
Dolle et al.	EP-A-0 628 550	December 14, 1994
Dolle et al.	EP-A-0 644 197	March 22, 1995
Dolle et al.	EP-A-0 644 198	March 22, 1995
Dolle et al.	AU-A-64514/94	December 8, 1994

Publications

- M. Ator, "Peptide and Non-peptide Inhibitors of Interleukin-1β Converting Enzyme", <u>Cambridge Healthtech Institute (Inflammatory Cytokine Antagonists Targets, Strategies, and Indication)</u>,(1994).
- M.A. Ator and R.E. Dolle, "Interleukin-1β Converting Enzyme: Biology and the Chemistry of Inhibitors", <u>Curr. Pharm. Design</u>, 1, pp. 191-210 (1995).
- M. Barinaga, "Death Gives Birth to the Nervous System. But How?", <u>Science</u>, 259, pp. 762-763 (1993).
- P. Bender & J. Lee, "Pharmacological Modulation of Interleukin-1", <u>Annu. Rep. Med. Chem.</u>, 25, pp. 185-193 (1989).
- R. Black et al., "Activation of Interleukin-1β by a Co-induced Protease", <u>FEBS Lett.</u>, 247, pp. 386-390 (1989).
- J. Breitner et al., "Inverse Association of Anti-inflammatory Treatments and Alzheimer's Disease: Initial Results of a Co-twin Control Study", Neurology, 44, pp. 227-232 (1994).
- F. Casano et al., "The Structure and Complete Nucleotide Sequence of the Murine Gene Encoding Interleukin-1β Converting Enzyme (ICE)", <u>Genomics</u>, 20, pp. 474-481 (1994).
- D. Cerretti et al., "Molecular Cloning of the Interleukin-1β Converting Enzyme", <u>Science</u>, 256, pp. 97-100 (1992).
- K. Chapman, "Synthesis of a Potent, Reversible Inhibitor of Interleukin-1β Converting Enzyme", Bioorg. Med. Chem. Lett., 2, pp. 613-618 (1992).

- C. Dinarello, "Role of Interleukin-1 in Infectious Diseases", <u>Immunol. Rev.</u>, 127, pp. 119-146 (1992).
- C. Dinarello et al., "Anticytokine Strategies in the Treatment of the Systemic Inflammatory Response Syndrome", J. Am. Med. Assoc., 269, pp. 1829-1835 (1993).
- R. Dolle et al., "Aspartyl α -((1-Phenyl-3-(trifluoromethyl)-pyrazol-5-yl)oxy)methyl Ketones as Interleukin-1 β Converting Enzyme Inhibitors. Significance of the P_1 and P_3 Amido Nitrogens for Enzyme-Peptide Inhibitor Binding", <u>J. Med. Chem.</u>, 37, pp. 3863-3865 (1994).
- R. Dolle et al., "Aspartyl α -((Diphenylphosphinyl)oxy)methyl Ketones as Novel Inhibitors of Interleukin-1 β Converting Enzyme. Utility of the Diphenylphosphinic Acid Leaving Group for the Inhibition of Cysteine Proteases", J. Med. Chem., 38, pp. 220-222 (1995).
- R. Dolle et al., " P_1 Aspartate-Based Peptide α -((2,6-Dichlorobenzoyl)oxy)methyl Ketones as Potent Time-Dependent Inhibitors of Interleukin-1 β -Converting Enzyme", <u>J. Med. Chem.</u>, 37, pp. 563-564 (1994).
- P. Edwards et al., "Design, Synthesis, and Kinetic Evaluation of a Unique Class of Elastase Inhibitors, the Peptidyl α-Ketobenzoxazoles, and the X-ray Crystal Structure of the Covalent Complex between Porcine Pancreatic Elastase and Ac-Ala-Pro-Val-2-Benzoxazole", <u>J. Am. Chem. Soc.</u>, 114, pp. 1854-1863 (1992).
- T. Fan et al., "Stimulation of Angiogenesis by Substance P and Interleukin-1 in the Rat and Its Inhibition by NK₁ or Interleukin-1 Receptor Antagonists", <u>Br. J. Pharmacol.</u>, 110, pp. 43-49 (1993).
- I. Fauszt et al., "Inhibition of Interleukin-1β Converting Enzyme by Peptide Derivatives", <u>Proc. of the 13th Am. Peptide Symp.</u>, June 20-25, 1993, Hodges, R.S. and Smith, J.A., Eds., <u>Peptides</u>, pp. 589-591 (1994).
- D.S. Fletcher, et al., "A Synthetic Inhibitor of Interleukin-1 β Converting Enzyme Prevents Endotoxin-Induced Interleukin-1 β Production In Vitro and In Vivo," J. Interfer. Cytokine Res., 15, pp. 243-248 (1995).
- V. Gagliardini et al., "Prevention of Vertebrate Neuronal Death by the crmA Gene", <u>Science</u>, 263, pp. 826-828 (1994).
- T. Geiger et al., "Neutralization of Interleukin-1β Activity in vivo with a Monoclonal Antibody Alleviates Collagen-induced Arthritis in DBA/1 Mice and Prevents the Associated Acute-phase Response", Clin. Exp. Rheumatol., 11, pp. 515-522 (1993).

- T. Graybill et al., "The Preparation and Evaluation of Peptidic Aspartyl Hemiacetals as Reversible Inhibitors of ICE", Am. Chem. Soc. Abs. (206th Natl. Mtg.), MEDI 235 (1993).
- T. Graybill et al., "Preparation and Evaluation of Peptidic Aspartyl Hemiacetals as Reversible Inhibitors of Interleukin-1β converting enzyme (ICE)", <u>Int. J. Peptide Protein Res.</u>, 44, pp. 173-182 (1994).
- T. Graybill et al., "Synthesis and Evaluation of Diacylhydrazines as Inhibitors of the Interleukin-1β Converting Enzyme (ICE)", <u>Bioorg. Med. Chem. Lett.</u>, 5, pp. 1197-1202 (1995).
- W. Griffin et al., "Brain Interleukin 1 and S-100 Immunoreactivity are Elevated in Down Syndrome and Alzheimer Disease", <u>Proc. Natl. Acad. Sci. USA</u>, 86, pp. 7611-7615 (1989).
- C. Hammerberg et al., "Interleukin-1 Receptor Antagonist in Normal and Psoriatic Epidermis", <u>J.</u> <u>Clin. Invest.</u>, 90, pp. 571-583 (1992).
- S. Hanessian et al., "Design and Synthesis of a Prototype Model Antagonist of Tachykinin NK-2 Receptor", <u>Biorg. Med. Chem. Lett.</u>, 3, pp. 2689-2692 (1993).
- E. Harris, "Rheumatoid Arthritis: Pathophysiology and Implications for Therapy", N. Eng. J. Med., 322, pp. 1277-1289 (1990).
- A. Howard et al., "High-Level Production and Characterization of Functional Human Interleukin-1β Converting Enzyme in Baculovirus and E. coli Expression Systems", <u>J. Cell. Biochem.</u> Suppl., 17B, p. 146 (1993).
- A. Howard et al., "Human Interleukin-1β Converting Enzyme: A Mutational Analysis of Proenzyme Activation", J. Cell. Biochem. Suppl., 17B, p. 113 (1993).
- A. Howard et al., "IL-1-Converting Enzyme Requires Aspartic Acid Residues for Processing of the IL-1β Precursor at Two Distinct Sites and Does Not Cleave 31-kDa IL-1α", <u>J. Immunol.</u>, 147, pp. 2964-2969 (1991).
- I. Kamphuis et al., "Thiol Proteases: Comparative Studies Based on the High-resolution Structures of Papain and Actinidin, and on Amino Acid Sequence Information for Cathepsins B and H, and Stem Bromelain", J. Mol. Biol., 182, pp. 317-329 (1985).
- M. Kostura et al., "Identification of a Monocyte Specific Pre-Interleukin 1β Convertase Activity", Proc. Natl. Acad. Sci. USA, 86, pp. 5227-5231 (1989).
- K. Kuida et al., "Altered Cytokine Export and Apoptosis in Mice Deficient in Interleukin-1β Converting Enzyme", <u>Science</u>, 267, pp. 2000-2003 (1995).

- P. Li et al., "Mice Deficient in IL-1β-Converting Enzyme are Defective in Production of Mature IL-1β and Resistant to Endotoxic Shock", Cell, 80, pp. 401-411 (1995).
- C. Lipinski, "Bioisosterism in Drug Design", Annu. Rep. Med. Chem., 21, pp. 283-291 (1986).
- G. Lonnemann et al., "Differences in the Synthesis and Kinetics of Release of Interleukin 1α , Interleukin 1β and Tumor Necrosis Factor from Human Mononuclear Cells", <u>Eur. J. Immunol.</u>, 19, pp. 1531-1536 (1989).
- A. MacKenzie et al., "An Inhibitor of the Interleukin-1β-Processing Enzyme Blocks IL-1 Release and Reduces Pyrexia and Acute Inflammation", <u>Inflammation Research Association (7th Internat. Conf.)</u>, W42 (1994).
- T. Mandrup-Poulsen et al., "Involvement of Interleukin 1 and Interleukin 1 Antagonist in Pancreatic β-Cell Destruction in Insulin-dependent Diabetes Mellitus", <u>Cytokine</u>, 5, pp. 185-191 (1993).
- C. March et al., "Cloning, Sequence and Expression of Two Distinct Human Interleukin-1 Complementary DNAs", Nature, 315, pp. 641-647 (1985).
- J. Marx, "Cell Death Studies Yield Cancer Clues", Science, 259, pp. 760-761 (1993).
- D. Miller et al., "The IL-1β Converting Enzyme as a Therapeutic Target", <u>Ann. N. Y. Acad. Sci.</u>, 696, pp. 133-148 (1993).
- B. Miller et al., "Inhibition of Mature IL-1 β Production in Murine Macrophages and a Murine Model of Inflammation by WIN 67694, an Inhibitor of IL-1 β Converting Enzyme", <u>J. Immunol.</u>, 154, pp. 1331-1338 (1995).
- M. Miura et al., "Induction of Apoptosis in Fibroblasts by IL-1β-Converting Enzyme, a Mammalian Homolog of the C.elegans Cell Death Gene ced-3", Cell, 75, pp. 653-660 (1993).
- A. Mjalli et al., "Phenylalkyl Ketones as Potent Reversible Inhibitors of Interleukin-1β Converting Enzyme", <u>Bioorg. Med. Chem. Lett.</u>, 3, pp. 2689-2692 (1993).
- A. Mjalli et al., "Activated Ketones as Potent Reversible Inhibitors of Interleukin-1β Converting Enzyme", <u>Bioorg. Med. Chem. Lett.</u>, 4, pp. 1965-1968 (1994).
- S. Molineaux et al., "Interleukin 1β (IL-1β) Processing in Murine Macrophages Requires a Structurally Conserved Homologue of Human IL-1β Converting Enzyme", <u>Proc. Natl. Acad. Sci. USA</u>, 90, pp. 1809-1813 (1993).

- B. Mosley et al., "Determination of the Minimum Polypeptide Lengths of the Functionally Active Sites of Human Interleukins 1α and 1β ", <u>Proc. Natl. Acad. Sci. USA</u>, 84, pp. 4572-4576 (1987).
- M. Mullican et al., "The Synthesis and Evaluation of Peptidyl Aspartyl Aldehydes as Inhibitors of ICE", <u>Bioorg. Med. Chem. Lett.</u>, 4, pp. 2359-2364 (1994).
- C. Nalin, "Apoptosis Research Enters the ICE Age", Structure, 3, pp. 143-145 (1995).
- M. Nett et al., "Molecular Cloning of the Murine IL-1β Converting Enzyme cDNA", <u>J.</u> Immunol., 149, pp. 3254-3259 (1992).
- M. Nett-Fiordalisi et al., "Characterization and Activation of the Murine Interleukin-1β (IL-1β) Converting Enzyme", J. Cell. Biochem. Suppl., 17B, p. 117 (1993).
- I. Noronha et al., "In situ Production of TNF- α , IL-1 β and IL-2R in ANCA-positive Glomerulonephritis", <u>Kidney Int.</u>, 43, pp. 682-692 (1993).
- K. Ohlsson et al., "Interleukin-1 Receptor Antagonist Reduces Mortality from Endotoxin Shock", Nature, 348, pp. 550-552 (1990).
- J. Oppenheim et al., "There is More than One Interleukin 1", <u>Immunol. Today</u>, 7, pp. 45-55 (1986).
- M. Pennington & N. Thornberry, "Synthesis of a Fluorogenic Interleukin-1β Converting Enzyme Substrate Based on Resonance Energy Transfer", <u>Pept. Res.</u>, 7, pp. 72-76 (1994).
- L. Polgár, "On the Mode of Activation of the Catalytically Essential Sulfhydryl Group of Papain", <u>Eur. J. Biochem.</u>, 33, pp. 104-109 (1973).
- C. Prasad et al., "P₁ Aspartate-Based Peptide α -Arylacyloxy- and α -Aryloxymethyl Ketones as Potent Time-Dependent Inhibitors of Interleukin 1 β Converting Enzyme", <u>Am. Chem. Soc. Abs.</u> (24th Med. Chem. Symp.), 66 (1994).
- C. Ray et al., "Viral Inhibition of Inflammation: Cowpox Virus Encodes an Inhibitor of the Interleukin-1β Converting Enzyme", Cell, 69, pp. 597-604 (1992).
- L. Reiter, "Peptidic p-Nitroanilide Substrates of Interleukin-1β-Converting Enzyme", <u>Int. J. Pept. Protein Res.</u>, 43, pp. 87-96 (1994).
- L. Revesz et al., "Synthesis of P1 Aspartate-Based Peptide Acyloxymethyl and Fluoromethyl Ketones as Inhibitors of Interleukin-1β-Converting Enzyme", <u>Tetrahedron Lett.</u>, 35, pp. 9693-9696 (1994).

- R. Robinson and K. Donahue, "Synthesis of a Peptidyl Difluoro Ketone Bearing the Aspartic Acid Side Chain: An Inhibitor of Interleukin-1β Converting Enzyme", <u>J. Org. Chem.</u>, 57, pp. 7309-7314 (1992).
- M. Salvatore et al., "L-741,494, A Fungal Metabolite that is an Inhibitor of Interleukin-1β Converting Enzyme", J. Nat. Prods., 57, pp. 755-760 (1994).
- J. Sandberg et al., "Treatment with an Interleukin-1 Receptor Antagonist Protein Prolongs Mouse Islet Allograft Survival", <u>Diabetes</u>, 42, pp. 1845-1851 (1993).
- S. Schmidt et al., "Synthesis and Evaluation of Aspartyl α-Chloro-, α-Aryloxy-, and α-Arylacyloxymethyl Ketones as Inhibitors of Interleukin-1β Converting Enzyme", <u>Am. Chem.</u> Soc. Abs. (208th Natl. Mtg.), MEDI 4, (1994).
- B. Shivers et al., "Molecular Cloning of Rat Interleukin-1β-Converting Enzyme: Distribution and Regulation", J. Cell. Biochem. Suppl., 17B, p. 119 (1993).
- I. Singer et al., "Interleukin 1β is Localized in the Cytoplasmic Ground Substance but is Largely Absent from the Golgi Apparatus and Plasma Membranes of Stimulated Human Monocytes", <u>J. Exp. Med.</u>, 167, pp. 389-407 (1988).
- P. Sleath et al., "Substrate Specificity of the Protease that Processes Human Interleukin-1β", <u>J.</u> <u>Biol. Chem.</u>, 265, pp. 14526-14528 (1990).
- A.F. Spatola, <u>Chemistry and Biochemistry of Amino Acids</u>, <u>Peptides and Proteins</u>, Vol. 7 (Weinstein, Ed., Dekker Inc.) pp. 267-281 (1983).
- N. Thornberry et al., "A Novel Heterodimeric Cysteine Protease is Required for Interleukin-1β Processing in Monocytes", <u>Nature</u>, 356, pp. 768-774 (1992).
- N. Thornberry et al., "Inactivation of Interleukin-1β Converting Enzyme by Peptide (Acyloxy)methyl Ketones", <u>Biochemistry</u>, 33, pp. 3934-3940 (1994).
- J. Uhl et al., "Secretion of Human Monocyte Mature IL-1β: Optimization of Culture Conditions and Inhibition by ICE Inhibitors", <u>Inflammation Research Association (7th Internat. Conf.)</u>, W41 (1994).
- N.P.C. Walker et al., "Crystal Structure of the Cysteine Protease Interleukin- 1β -Converting Enzyme: A $(p20/p10)_2$ Homodimer", <u>Cell</u>, 78, pp. 343-352 (1994).
- P. Warner, et al., "Pyridone HLE Inhibitors: Variation of the 3 and 5 Substituents", <u>Royal Soc. Chem. Abs. (7th RSC-SCI Med. Chem. Symp.)</u>, P23 (1993).

- K.P. Wilson, et al., "Structure and Mechanism of Interleukin-1β Converting Enzyme", <u>Nature</u>, 370, pp. 270-275 (1994).
- P. Wooley et al., "The Effect of an Interleukin-1 Receptor Antagonist Protein on Type II Collagen-induced Arthritis and Antigen-induced Arthritis in Mice", <u>Arthritis Rheum.</u>, 36, pp. 1305-1314 (1993).
- J. Yuan et al., "The C.elegans Cell Death Gene ced-3 Encodes a Protein Similar to Mammalian Interleukin-1β-Converting Enzyme", Cell, 75, pp. 641-652 (1993).

The above-mentioned documents are listed on the accompanying Form PTO-1449 (submitted in duplicate). Applicants submitted copies of these documents in United States application 08/598,332, filed February 8, 1996 (now patent no. 5,874,424), and United States application 08/761,483, filed December 6, 1996 (now patent no. 6,204,261), from which this application claims priority. Applicants cited these documents in United States application 09/400,639, filed September 21, 1999 (now patent no. 6,258,948) and United States application 09/773,477, filed January 31, 2001 (now patent no. 6,423,840), from which this application also claims priority. Accordingly, pursuant to 37 C.F.R. § 1.98(d), applicants have not provided copies of these documents herewith.

Applicants respectfully request that the above-cited documents be (1) fully considered by the Examiner during the course of the examination of this application and (2) printed on any patent issuing from this application. Applicants also request that a copy of the enclosed Form PTO-1449 duly initialed by the Examiner be forwarded to the undersigned with the next communication.

The Director is hereby authorized to charge payment of any fees required in connection with this Information Disclosure Statement to Deposit Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

Respectfully submitted,

James F. Haley (Reg. No. 27,794)

Attorney for Applicants

Min Wang (Reg. No. 51,303)

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Sheet _1_ of _8_

#3

FORM PTO-1449 U.S. DEFÄRTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

ATTY. DOCKET NO. VPI/96-01 CIP2 DIV3

APPLICATION NO. 10/058,522

APPLICANT

CONFIRMATION

Mark James Batchelor, et al.

4312

FILING DATE January 28, 2002 GROUP 1624

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,276,298	6/30/81	Jones et al.	424	270	
	4,369,183	1/18/83	Jones et al.	424	263	RECEIVED
	4,499,295	2/12/85	Mueller et al.	560	53	HEVEIVEL
	4,551,279	11/5/85	Mueller et al.	260	404	AUG 0 5 2002
	4,584,397	4/22/86	Mueller et al.	560	75	
	4,968,607	11/6/90	Dower et al.	435	69.1 T	ECH CENTER 1600/29
	5,008,245	4/16/91	Digenis et al.	514	18	
····	5,055,451	10/8/91	Krantz et al.	514	19	
	5,081,228	1/14/92	Dower et al.	530	35.1	
	5,158,936	10/27/92	Krantz et al.	514	19	
	5,180,812	1/19/93	Dower et al.	530	351	
	5,374,623	12/20/94	Zimmerman et al.	514	17	
	5,411,985	5/2/95	Bills et al.	514	460	
	5,416,013	5/16/95	Black et al.	435	226	
<u>- </u>	5,430,128	7/4/95	Chapman et al.	530	330	
	5,434,248	7/18/95	Chapman et al.	530	330	
	5,462,939	10/31/95	Dolle et al.	514	231.5	
	5,486,623	01/23/96	Zimmerman et al.	549	417	12/08/93
	5,498,616	03/12/96	Mallamo et al.	514	300	11/04/94
	5,498,695	03/12/96	Daumy et al.	530	331	12/12/94
	5,552,400	09/03/96	Dolle et al.	514	221	06/08/94
	5,565,430	10/15/96	Dolle et al.	514	19	08/02/94
	5,656,627	8/12/97	Bemis	514	221	3/17/95
	5,716,929	2/10/98	Bemis	514	18	6/5/95
	5,756,466	5/26/98	Bemis	514	18	6/17/94
	5,585,357	12/17/96	Dolle	544	182	1/29/96
	5,585,486	12/17/96	Dolle	544	182	5/12/95
	5,670,494	9/23/97	Dolle	514	86	11/20/95
	5,639,745	6/17/97	Dolle	514	183	5/25/95

EXAMINER DATE CONSIDERED

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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SERIAL NO. 09/400,639

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Mark James Batchelor, et al.

FILING DATE September 21, 1999 GROUP 1614

FOREIGN PATENT DOCUMENTS

EXAMINER	MINER		OOLINITES/		OLIBOLAGO	TRANSLATION	
INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	YES	NO
	WO 90/13549	11/15/90	PCT	C07D	417/06		
	WO 91/15577	10/17/91	PCT	C12N	9/64		
	WO 93/05071	3/18/93	PCT	C07K	13/00		
	WO 93/09135	5/13/93	PCT	C07K	5/04		
	WO 93/14777	8/5/93	PCT	A61K	37/00		
	WO 93/16710	9/2/93	PCT	A61K	37/00		
	WO 93/25683	12/23/93	PCT	C12N	15/12		
	WO 93/25685	12/23/93	PCT	C12N	15/12		
	WO 93/25694	12/23/93	PCT	C12N	15/57		
	WO 94/00154	1/6/94	PCT	A61K	39/395		
	WO 94/03480	2/17/94	PCT	C07K	5/02		
	WO 95/00160	1/5/95	PCT	A61K	37/02		
	WO 95/05192	2/23/95	PCT	A61K	38/06		
	WO 95/16706	6/22/95	PCT	C07K	14/54		
	WO 95/26958	10/12/95	PCT	C07D	239/47		
· 	WO 95/29672	11/9/95	PCT	A61K	031/16		
	WO 95/33751	12/14/95	PCT	C07D	487/04		
	WO 95/35308	12/28/95	PCT	C07K	5/023		
	WO 96/03982	2/15/96	PCT	A61K	31/15		
	WO 96/25408	8/22/96	PCT	C07D	305/08		
	EP-A-0 275 101	7/20/88	EPO	C07K	5/02		
	EP-A-0 410 411	1/30/91	EPO	C07K	5/04		
	EP-A-0 417 721	3/20/91	EPO	C07K	5/10		
	EP-A-0 479 489	4/8/92	EPO	C07K	5/08		
	EP-A-0 504 938	9/23/92	EPO	A61K	37/02		
	EP-A-0 519 748	12/23/92	EPO	C07K	5/04		
	EP-A-0 525 420	2/3/93	EPO	C07D	307/56		
	EP-A-0 528 487	2/24/93	EPO	C07K	5/10		
	EP-A-0 529 713	3/3/93	EPO	B01J	20/32		
	EP-A-0 533 226	3/24/93	EPO	C07K	5/10		

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	EP-A-0 618 223	10/5/94	EPO	C07K	5/02	TLO	IVED
	EP-A-0 623 606	11/9/94	EPO	C07D	307/60		5 2002
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•	EP-A-0 644 197	3/22/95	EPO	C07K	5/02 IE	CH CENTE	R 1600/2900
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/ JUL 2 9 2002	INFORMATION DISCLOSURE	APPLICANT Mark James Batchelor, et al.				
	STATEMENT BY APPLICANT	FILING DATE September 21, 1999	GROUP 1614			
DADEMAR	OTHER DOCUMENTS (Including Author, Titl	e, Date, Pertinent Pages, Etc.)				
EXAMINER INITIAL						
	M. Ator, "Peptide and Non-peptide Inhibitors of Inte Healthtech Institute (Inflammatory Cytokine Antago					
	M.A. Ator and R.E. Dolle, "Interleukin-1β Convertir Inhibitors", Curr. Pharm. Design, 1, pp. 191-210 (19		emistry of			
	M. Barinaga, "Death Gives Birth to the Nervous Sy (1993)	stem. But How?", <u>Science,</u> 25	9, pp. 762-763			
	P. Bender & J. Lee, "Pharmacological Modulation of 185-193 (1989)	of Interleukin-1", <u>Annu. Rep. Me</u>	ed. Chem., 25, pp.			
	R. Black et al., "Activation of Interleukin-1 β by a Co (1989)	o-induced Protease", <u>FEBS Let</u>	<u>t.,</u> 247, pp. 386-390			
	J. Breitner et al., "Inverse Association of Anti-inflam Initial Results of a Co-twin Control Study", <u>Neurolo</u>	nmatory Treatments and Alzhei gy, 44, pp. 227-232 (1994)	mer's Disease:			
	F. Casano et al., "The Structure and Complete Nucl Interleukin-1β Converting Enzyme (ICE)", <u>Genomic</u>	ure and Complete Nucleotide Sequence of the Murine Gene Encoding zyme (ICE)", Genomics, 20, pp. 474-481 (1994)				
	D. Cerretti et al., "Molecular Cloning of the Interleukin-1 β Converting Enzyme", Science, 256, pp. 97-100 (1992)					
	K. Chapman, "Synthesis of a Potent, Reversible In Bioorg. Med. Chem. Lett., 2, pp. 613-618 (1992)	hibitor of Interleukin-1β Conver	ting Enzyme",			
	C. Dinarello, "Role of Interleukin-1 in Infectious Diseases", Immunol. Rev., 127, pp. 119-146 (1992)					
	C. Dinarello et al., "Anticytokine Strategies in the Treatment of the Systemic Inflammatory Resp Syndrome", <u>J. Am. Med. Assoc.</u> , 269, pp. 1829-1835 (1993) R. Dolle et al., "Aspartyl α-((1-Phenyl-3-(trifluoromethyl)-pyrazol-5-yl)oxy)methyl Ketones as Interleukin-1β Converting Enzyme Inhibitors. Significance of the P ₁ and P ₃ Amido Nitrogens for Enzyme-Peptide Inhibitor Binding", <u>J. Med. Chem.</u> , 37, pp. 3863-3865 (1994)					
R. Dolle et al., "Aspartyl α-((Diphenylphosphinyl)oxy)methyl Ketones as Novel Inhibitors of Into 1β Converting Enzyme. Utility of the Diphenylphosphinic Acid Leaving Group for the Inhibition Cysteine Proteases", J. Med. Chem., 38, pp. 220-222 (1995)						
	R. Dolle et al., "P ₁ Aspartate-Based Peptide α-((2,6					

EXAMINER

(1994)

1863 (1992)

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

P. Edwards et al., "Design, Synthesis, and Kinetic Evaluation of a Unique Class of Elastase Inhibitors, the Peptidyl α -Ketobenzoxazoles, and the X-ray Crystal Structure of the Covalent Complex between Porcine Pancreatic Elastase and Ac-Ala-Pro-Val-2-Benzoxazole", <u>J. Am. Chem. Soc.</u>, 114, pp. 1854-

FORM PTO-14	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. VPI96-01 CIP2 DIV	SERIAL NO. 09/400,639		
Since of	INFORMATION DISCLOSURE	APPLICANT Mark James Batchelor, et al.			
JUL 2 9 2002 EXAMINER	STATEMENT BY APPLICANT	FILING DATE September 21, 1999	GROUP 1614		
The maneral B	OTHER DOCUMENTS (Including Author, Title,	Date, Pertinent Pages, Etc.)			
EXAMINER INITIAL					
	T. Fan et al., "Stimulation of Angiogenesis by Substance P and Interleukin-1 in the Rat and Its Inhibition by NK ₁ or Interleukin-1 Receptor Antagonists", <u>Br. J. Pharmacol.</u> , 110, pp. 43-49 (1993)				
	 I. Fauszt et al., "Inhibition of Interleukin-1β Converting Enzyme by Peptide Derivatives", Proc. of the 13th Am. Peptide Symp., June 20-25, 1993, Hodges, R.S. and Smith, J.A., Eds., Peptides, pp. 589-591 (1994) D.S. Fletcher, et al., "A Synthetic Inhibitor of Interleukin-1β Converting Enzyme Prevents Endotoxin-Induced Interleukin-1β Production In Vitro and In Vivo," J. Interfer. Cytokine Res., 15, pp. 243-248 (1995). V. Gagliardini et al., "Prevention of Vertebrate Neuronal Death by the crmA Gene", Science, 263, pp. 826-828 (1994) T. Geiger et al., "Neutralization of Interleukin-1β Activity in vivo with a Monoclonal Antibody Alleviates Collagen-induced Arthritis in DBA/1 Mice and Prevents the Associated Acute-phase Response", Clin. Exp. Rheumatol., 11, pp. 515-522 (1993) T. Graybill et al., "The Preparation and Evaluation of Peptidic Aspartyl Hemiacetals as Reversible Inhibitors of ICE", Am. Chem. Soc. Abs. (206th Natl. Mtg.), MEDI 235 (1993) T. Graybill et al., "Preparation and Evaluation of Peptidic Aspartyl Hemiacetals as Reversible Inhibitors of Interleukin-1β Cnverting Enzyme (ICE)", Int. J. Peptide Protein Res., 44, pp. 173-182 (1994) T. Graybill et al., "Synthesis and Evaluation of Diacylhydrazines as Inhibitors of the Interleukin-1β Converting Enzyme (ICE)", Bioorg. Med. Chem. Lett., 5, pp. 1197-1202 (1995). 				
	 W. Griffin et al., "Brain Interleukin 1 and S-100 Immunoreactivity are Elevated in Down Syndrome and Alzheimer Disease", Proc. Natl. Acad. Sci. USA, 86, pp. 7611-7615 (1989) C. Hammerberg et al., "Interleukin-1 Receptor Antagonist in Normal and Psoriatic Epidermis", J. Clin. Invest., 90, pp. 571-583 (1992) S. Hanessian et al., "Design and Synthesis of a Prototype Model Antagonist of Tachykinin NK-2 Receptor", Biorg. Med. Chem. Lett., 3, pp. 2689-2692 (1993) E. Harris, "Rheumatoid Arthritis: Pathophysiology and Implications for Therapy", N. Eng. J. Med., 322, pp. 1277-1289 (1990) 				
	A. Howard et al., "High-Level Production and Characterization of Functional Human Interleukin-1β Converting Enzyme in Baculovirus and E. coli Expression Systems", <u>J. Cell. Biochem. Suppl.</u> , 17B, 146 (1993)				
	A. Howard et al., "Human Interleukin-1β Converting Enzyme: A Mutational Analysis of Proenzyme Activation", <u>J. Cell. Biochem. Suppl.</u> , 17B, p. 113 (1993)				
	A. Howard et al., "IL-1-Converting Enzyme Requires Aspartic Acid Residues for Processing of the IL-1β Precursor at Two Distinct Sites and Does Not Cleave 31-kDa IL-1α", <u>J. Immunol.</u> , 147, pp. 2964-				

EXAMINER

2969 (1991)

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.



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FILING DATE September 21, 1999 GROUP 1614

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

JUL 2 9 2002

EXAMINER			
INITIAL	I. Kamphuis et al., "Thiol Proteases: Comparative Studies Based on the High-resolution Structures of Papain and Actinidin, and on Amino Acid Sequence Information for Cathepsins B and H, and Stem Bromelain", J. Mol. Biol., 182, pp. 317-329 (1985)		
	M. Kostura et al., "Identification of a Monocyte Specific Pre-Interleukin 1β Convertase Activity", Proc Natl. Acad. Sci. USA, 86, pp. 5227-5231 (1989)		
	K. Kuida et al., "Altered Cytokine Export and Apoptosis in Mice Deficient in Interleukin-1β Converting Enzyme", Science, 267, pp. 2000-2003 (1995)		
	P. Li et al., "Mice Deficient in IL-1β-Converting Enzyme are Defective in Production of Mature IL-1β and Resistant to Endotoxic Shock", <u>Cell</u> , 80, pp. 401-411 (1995)		
	C. Lipinski, "Bioisosterism in Drug Design", Annu. Rep. Med. Chem., 21, pp. 283-291 (1986)		
	G. Lonnemann et al., "Differences in the Synthesis and Kinetics of Release of Interleukin 1α , Interleukin 1β and Tumor Necrosis Factor from Human Mononuclear Cells", <u>Eur. J. Immunol.</u> , 19, pp. 1531-1536 (1989)		
	A. MacKenzie et al., "An Inhibitor of the Interleukin-1β-Processing Enzyme Blocks IL-1 Release and Reduces Pyrexia and Acute Inflammation", <u>Inflammation Research Association (7th Internat. Conf.)</u> , W42 (1994)		
	T. Mandrup-Poulsen et al., "Involvement of Interleukin 1 and Interleukin 1 Antagonist in Pancreatic β-Cell Destruction in Insulin-dependent Diabetes Mellitus", <u>Cytokine</u> , 5, pp. 185-191 (1993)		
	C. March et al., "Cloning, Sequence and Expression of Two Distinct Human Interleukin-1 Complementary DNAs", Nature, 315, pp. 641-647 (1985)		
	J. Marx, "Cell Death Studies Yield Cancer Clues", Science, 259, pp. 760-761 (1993)		
	D. Miller et al., "The IL-1β Converting Enzyme as a Therapeutic Target", Ann. N. Y. Acad. Sci., 696, pp. 133-148 (1993)		
	B. Miller et al., "Inhibition of Mature IL-1β Production in Murine Macrophages and a Murine Model of Inflammation by WIN 67694, an Inhibitor of IL-1β Converting Enzyme", <u>J. Immunol.</u> , 154, pp. 1331-1338 (1995)		
	M. Miura et al., "Induction of Apoptosis in Fibroblasts by IL-1β-Converting Enzyme, a Mammalian Homolog of the C.elegans Cell Death Gene ced-3", <u>Cell</u> , 75, pp. 653-660 (1993)		
	A. Mjalli et al., "Phenylalkyl Ketones as Potent Reversible Inhibitors of Interleukin-1β Converting Enzyme", Bioorg. Med. Chem. Lett., 3, pp. 2689-2692 (1993)		
	A. Mjalli et al., "Activated Ketones as Potent Reversible Inhibitors of Interleukin-1β Converting Enzyme", Bioorg. Med. Chem. Lett., 4, pp. 1965-1968 (1994)		

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.



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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

70T 5 3 5005

OTHER DOCUMENTS (Including-Atthor, Title, Date, Pertinent Pages, Etc.)			
EXAMINER INITIAL			
	S. Molineaux et al., "Interleukin 1β (IL-1β) Processing in Murine Macrophages Requires a Structurally Conserved Homologue of Human IL-1β Converting Enzyme", <u>Proc. Natl. Acad. Sci. USA</u> , 90, pp. 1809-1813 (1993)		
	B. Mosley et al., "Determination of the Minimum Polypeptide Lengths of the Functionally Active Sites of Human Interleukins 1α and 1β", Proc. Natl. Acad. Sci. USA, 84, pp. 4572-4576 (1987)		
	M. Mullican et al., "The Synthesis and Evaluation of Peptidyl Aspartyl Aldehydes as Inhibitors of ICE", Bioorg. Med. Chem. Lett., 4, pp. 2359-2364 (1994)		
	C. Nalin, "Apoptosis Research Enters the ICE Age", <u>Structure</u> , 3, pp. 143-145 (1995).		
	M. Nett et al., "Molecular Cloning of the Murine IL-1β Converting Enzyme cDNA", <u>J. Immunol.</u> , 149, pp. 3254-3259 (1992)		
	M. Nett-Fiordalisi et al., "Characterization and Activation of the Murine Interleukin-1β (IL-1β) Converting Enzyme", <u>J. Cell. Biochem. Suppl.</u> , 17B, p. 117 (1993)		
	I. Noronha et al., "In situ Production of TNF- α , IL-1 β and IL-2R in ANCA-positive Glomerulonephritis", Kidney Int., 43, pp. 682-692 (1993)		
	K. Ohlsson et al., "Interleukin-1 Receptor Antagonist Reduces Mortality from Endotoxin Shock", Nature, 348, pp. 550-552 (1990)		
	J. Oppenheim et al., "There is More than One Interleukin 1", Immunol. Today, 7, pp. 45-55 (1986)		
	M. Pennington & N. Thornberry, "Synthesis of a Fluorogenic Interleukin-1β Converting Enzyme Substrate Based on Resonance Energy Transfer", Pept. Res., 7, pp. 72-76 (1994)		
	L. Polgár, "On the Mode of Activation of the Catalytically Essential Sulfhydryl Group of Papain", <u>Eur. J. Biochem.</u> , 33, pp. 104-109 (1973)		
	C. Prasad et al., "P ₁ Aspartate-Based Peptide α-Arylacyloxy- and α-Aryloxymethyl Ketones as Potent Time-Dependent Inhibitors of Interleukin 1β Converting Enzyme", <u>Am. Chem. Soc. Abs. (24th Med. Chem. Symp.)</u> , 66 (1994)		
	C. Ray et al., "Viral Inhibition of Inflammation: Cowpox Virus Encodes an Inhibitor of the Interleukin- 1β Converting Enzyme", <u>Cell</u> , 69, pp. 597-604 (1992)		
	L. Reiter, "Peptidic p-Nitroanilide Substrates of Interleukin-1β-Converting Enzyme", Int. J. Pept. Protein Res., 43, pp. 87-96 (1994)		
	L. Revesz et al., "Synthesis of P1 Aspartate-Based Peptide Acyloxymethyl and Fluoromethyl Ketones as Inhibitors of Interleukin-1β-Converting Enzyme", <u>Tetrahedron Lett.</u> , 35, pp. 9693-9696 (1994)		
	R. Robinson and K. Donahue, "Synthesis of a Peptidyl Difluoro Ketone Bearing the Aspartic Acid Side Chain: An Inhibitor of Interleukin-1β Converting Enzyme", J. Org. Chem., 57, pp. 7309-7314 (1992)		

EXAMINER

DATE CONSIDERED

FORM PTO-14		09/400,639				
INFORMATION DISCLOSURE PATENT AND TRADEMARK OF FIGE VPI96-01 CIP2 DIV 09/400,639 APPLICANT Whatk James Batchelor, et al.						
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	OTHER DOCUMENTS (Including Author, Pritie, Date, Pertinent Pages, Etc.)					
EXAMINER INITIAL						
	M. Salvatore et al., "L-741,494, A Fungal Metabolite that is an Inhibitor of Interleukin-1β Converting Enzyme", J. Nat. Prods., 57, pp. 755-760 (1994)					
	J. Sandberg et al., "Treatment with an Interleukin-1 Receptor Antagonist Protein Prolongs Mouse Islet Allograft Survival", <u>Diabetes</u> , 42, pp. 1845-1851 (1993)					
	S. Schmidt et al., "Synthesis and Evaluation of Aspartyl α-Chloro-, α-Aryloxy-, and α-Arylacyloxymethyl Ketones as Inhibitors of Interleukin-1β Converting Enzyme", <u>Am. Chem. Soc. Abs.</u> (208th Natl. Mtg.), MEDI 4 (1994)					
	B. Shivers et al., "Molecular Cloning of Rat Interleukin-1β-Converting Enzyme: Distribution and Regulation", J. Cell. Biochem. Suppl., 17B, p. 119 (1993)					
	I. Singer et al., "Interleukin 1β is Localized in the Cytoplasmic Ground Substance but is Largely Absent from the Golgi Apparatus and Plasma Membranes of Stimulated Human Monocytes", <u>J. Exp. Med.</u> , 167, pp. 389-407 (1988)					
	P. Sleath et al., "Substrate Specificity of the Protease that Processes Human Interleukin-1β", <u>J. Biol. Chem.</u> , 265, pp. 14526-14528 (1990)					
	A.F. Spatola, <u>Chemistry and Biochemistry of Amino Acids</u> , <u>Peptides and Proteins</u> , vol. 7, B. Weinstein, ed., Marcel Dekker Inc., ch. 5, pp. 267-281 (1983).					
	N. Thornberry et al., "A Novel Heterodimeric Cysteine Protease is Required for Interleukin-1β Processing in Monocytes", Nature, 356, pp. 768-774 (1992)					
	N. Thornberry et al., "Inactivation of Interleukin-1β Converting Enzyme by Peptide (Acyloxy)methyl Ketones", Biochemistry, 33, pp. 3934-3940 (1994)					
	J. Uhl et al., "Secretion of Human Monocyte Mature IL-1β: Optimization of Culture Conditions and Inhibition by ICE Inhibitors", Inflammation Research Association (7th Internat. Conf.), W41 (1994)					
	N.P.C. Walker et al., "Crystal Structure of the Cysteine Protease Interleukin-1β-Converting Enzyme: A (p20/p10) ₂ Homodimer", <u>Cell</u> , 78, pp. 343-352 (1994).					
	P. Warner, et al., "Pyridone HLE Inhibitors: Variation of the 3 and 5 Substituents", Royal Soc. Chem. Abs. (7th RSC-SCI Med. Chem. Symp.), P23 (1993)					
	K.P. Wilson et al., "Structure and Mechanism of Interleukin-1β Converting Enzyme", Nature, 370, pp. 270-275 (1994).					
	P. Wooley et al., "The Effect of an Interleukin-1 Receptor Antagonist Protein on Type II Collagen-induced Arthritis and Antigen-induced Arthritis in Mice", <u>Arthritis Rheum.</u> , 36, pp. 1305-1314 (1993)					
	J. Yuan et al., "The C.elegans Cell Death Gene ced-3 Encodes a Protein Similar to M Interleukin-1β-Converting Enzyme", <u>Cell</u> , 75, pp. 641-652 (1993)	ammalian				

EXAMINER

DATE CONSIDERED